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EXAMINER	
YANG, NELSON C	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/561,828	STOCK, JEFFRY B.	
	Examiner	Art Unit	
	Nelson Yang	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-62* is/are pending in the application.

4a) Of the above claim(s) *59-62* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 December 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of claims 1-58 in the reply filed on April 7, 2008 is acknowledged.

2. Claims 59-62 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on May 12, 2008.

Specification

3. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: the specification fails to provide support for methyaccepting chemosensory receptors recited in claims 39-41. Currently, it is believed that applicants meant to refer to methyl-accepting chemosensory receptors.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-3, 5-13, 15-23, 25-31, 35, 51-56 are rejected under 35 U.S.C. 102(b) as being anticipated by Daniels et al. [US 2002/0004246]. Daniels et al. teach a sensor comprising a first

detection reagent that binds to an analyte of interest and a capture agent that binds to first detection ligand. Daniels et al. also teach a second detection reagent that is capable of selectively binding a second target moiety of the analyte of interest (see entire patent).

In particular, with respect to claim 1, Daniels et al. teach a sensor comprising a first detection reagent comprising a ligand conjugated to a semiconductor nanocrystal (signaling moiety) that binds to a first target moiety of an analyte of interest (para. 0023, 0024, 0034, 0035), and a capture agent (sensing moiety) that binds to first detection ligand (para. 0025). Daniels et al. also teach a second detection reagent that is capable of selectively binding a second target moiety of the analyte of interest (para. 0035). It is further noted that the semiconductor nanocrystal is not a naturally occurring entity.

6. With respect to claim 2, Daniels et al. disclose a capture agent (sensing moiety) that binds to a first detection ligand (para. 0025), which would therefore bind to the target moiety indirectly.

7. With respect to claim 3, Daniels et al. teach a sensor comprising a first detection reagent comprising a ligand conjugated to a semiconductor nanocrystal (signaling moiety) that binds to a first target moiety of an analyte of interest (para. 0023, 0024, 0034, 0035), and a capture agent (sensing moiety) that binds to first detection ligand (para. 0025). Daniels et al. also teach a second detection reagent that is capable of selectively binding a second target moiety of the analyte of interest (para. 0035). Therefore different labels could bind to the different capture agents.

8. With respect to claims 5, 6, Daniels et al. teach a sensor comprising a first detection reagent comprising a ligand conjugated to a semiconductor nanocrystal (signaling moiety) that

binds to a first target moiety of an analyte of interest (para. 0023, 0024, 0034, 0035), and a capture agent (sensing moiety) that binds to first detection ligand (para. 0025). Daniels et al. also teach a second detection reagent that is capable of selectively binding a second target moiety of the analyte of interest (para. 0035). Daniels et al. further teach that this allows for detecting multiple analytes of interest and further quantitating the amount of a particular analyte present (para. 0121).

9. With respect to claim 7, Daniels et al. teach detecting multiple analytes of interest and further quantitating the amount of a particular analyte present (para. 0121). Therefore, the sensor of Daniels et al. would be capable of detecting first and second analytes of different concentrations. Furthermore, it is noted that the claims appear to be directed toward product-by-process limiations. "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)

10. With respect to claim 8, Daniels et al. teach recombinant production of antibody fragments (para. 0148), which is a form of de novo production. Furthermore, it is noted that the claims appear to be directed toward product-by-process limiations. "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the

prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)

11. With respect to claim 9, Daniels et al. teach that antibodies may be generated by in vitro immunization (para. 0144). Furthermore, it is noted that the claims appear to be directed toward product-by-process limiations. "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)

12. With respect to claim 10, Daniels et al. teach a sensor comprising a first detection reagent comprising a ligand conjugated to a semiconductor nanocrystal (signaling moiety) that binds to a first target moiety of an analyte of interest (para. 0023, 0024, 0034, 0035), and a capture agent (sensing moiety) that binds to first detection ligand (para. 0025). Thus the sensing and signaling moieties would be in different molecules or complexes.

13. With respect to claim 11, Daniels et al. teach a sensor comprising a first detection reagent comprising a ligand conjugated to a semiconductor nanocrystal (signaling moiety) that binds to a first target moiety of an analyte of interest (para. 0023, 0024, 0034, 0035), and a capture agent (sensing moiety) that binds to first detection ligand (para. 0025). Daniels et al. also teach a second detection reagent that is capable of selectively binding a second target moiety of the analyte of interest (para. 0035). It is further noted that the semiconductor nanocrystal is not a naturally occurring entity.

14. With respect to claim 12, Daniels et al. disclose a capture agent (sensing moiety) that binds to a first detection ligand (para. 0025), which would therefore bind to the target moiety indirectly.

15. With respect to claim 13, Daniels et al. teach a sensor comprising a first detection reagent comprising a ligand conjugated to a semiconductor nanocrystal (signaling moiety) that binds to a first target moiety of an analyte of interest (para. 0023, 0024, 0034, 0035), and a capture agent (sensing moiety) that binds to first detection ligand (para. 0025). Daniels et al. also teach a second detection reagent that is capable of selectively binding a second target moiety of the analyte of interest (para. 0035). Therefore different labels could bind to the different capture agents.

16. With respect to claims 15, 16, Daniels et al. teach a sensor comprising a first detection reagent comprising a ligand conjugated to a semiconductor nanocrystal (signaling moiety) that binds to a first target moiety of an analyte of interest (para. 0023, 0024, 0034, 0035), and a capture agent (sensing moiety) that binds to first detection ligand (para. 0025). Daniels et al. also teach a second detection reagent that is capable of selectively binding a second target moiety of the analyte of interest (para. 0035). Daniels et al. further teach that this allows for detecting multiple analytes of interest and further quantitating the amount of a particular analyte present (para. 0121).

17. With respect to claim 17, Daniels et al. teach detecting multiple analytes of interest and further quantitating the amount of a particular analyte present (para. 0121). Therefore, the sensor of Daniels et al. would be capable of detecting first and second analytes of different concentrations.

18. With respect to claim 18, Daniels et al. teach antibody fragments for binding members (para. 0090), which would be derived from the antigen binding site of an antibody.

19. With respect to claim 19, Daniels et al. teach that antibodies may be generated by in vitro immunization (para. 0144).

20. With respect to claim 20, Daniels et al. teach a sensor comprising a first detection reagent comprising a ligand conjugated to a semiconductor nanocrystal (signaling moiety) that binds to a first target moiety of an analyte of interest (para. 0023, 0024, 0034, 0035), and a capture agent (sensing moiety) that binds to first detection ligand (para. 0025). Thus the sensing and signaling moieties would be in different molecules or complexes.

21. With respect to claim 21, Daniels et al. teach a sensor comprising a first detection reagent comprising a ligand conjugated to a semiconductor nanocrystal (signaling moiety) that binds to a first target moiety of an analyte of interest (para. 0023, 0024, 0034, 0035), and a capture agent (sensing moiety) that binds to first detection ligand (para. 0025). Daniels et al. also teach a second detection reagent that is capable of selectively binding a second target moiety of the analyte of interest (para. 0035). It is noted that the semiconductor nanocrystal is not a naturally occurring entity. Daniels et al. further teach recombinant production of antibody fragments for use as capture agent for recognizing the analyte of interest (para. 0148), wherein recombinant techiniques are a form of de novo production.

22. It is also noted that the claims appear to be recite product-by-process limiations, specifically polypeptides that are formed from de novo processes. "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production.

If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)

23. With respect to claim 22, Daniels et al. disclose a capture agent (sensing moiety) that binds to a first detection ligand (para. 0025), which would therefore bind to the target moiety indirectly.

24. With respect to claim 23, Daniels et al. teach a sensor comprising a first detection reagent comprising a ligand conjugated to a semiconductor nanocrystal (signaling moiety) that binds to a first target moiety of an analyte of interest (para. 0023, 0024, 0034, 0035), and a capture agent (sensing moiety) that binds to first detection ligand (para. 0025). Daniels et al. also teach a second detection reagent that is capable of selectively binding a second target moiety of the analyte of interest (para. 0035). Therefore different labels could bind to the different capture agents.

25. With respect to claims 25, 26, Daniels et al. teach a sensor comprising a first detection reagent comprising a ligand conjugated to a semiconductor nanocrystal (signaling moiety) that binds to a first target moiety of an analyte of interest (para. 0023, 0024, 0034, 0035), and a capture agent (sensing moiety) that binds to first detection ligand (para. 0025). Daniels et al. also teach a second detection reagent that is capable of selectively binding a second target moiety of the analyte of interest (para. 0035). Daniels et al. further teach that this allows for detecting multiple analytes of interest and further quantitating the amount of a particular analyte present (para. 0121).

26. With respect to claim 27, Daniels et al. teach detecting multiple analytes of interest and further quantitating the amount of a particular analyte present (para. 0121). Therefore, the sensor of Daniels et al. would be capable of detecting first and second analytes of different concentrations.

27. With respect to claim 28, Daniels et al. teach antibody fragments for binding members (para. 0090), which would be derived from the antigen binding site of an antibody.

28. With respect to claim 29, Daniels et al. teach that antibodies may be generated by in vitro immunization (para. 0144).

29. With respect to claim 30, Daniels et al. teach a sensor comprising a first detection reagent comprising a ligand conjugated to a semiconductor nanocrystal (signaling moiety) that binds to a first target moiety of an analyte of interest (para. 0023, 0024, 0034, 0035), and a capture agent (sensing moiety) that binds to first detection ligand (para. 0025). Thus the sensing and signaling moieties would be in different molecules or complexes.

30. With respect to claim 31, Daniels et al. teach recombinant production of antibody fragments (para. 0148), which is a form of de novo production.

31. With respect to claim 35, Daniels et al. teach that the nanocrystals may be disposed in a nitrocellulose membrane (para. 0259).

32. With respect to claim 51, Daniels et al. teach antibody fragments for binding members (para. 0090), which would be derived from the antigen binding site of an antibody.

33. With respect to claim 52, Daniels et al. teach that antibodies may be generated by in vitro immunization (para. 0144).

34. With respect to claim 53, Daniels et al. teach a sensor comprising a first detection reagent comprising a ligand conjugated to a semiconductor nanocrystal (signaling moiety) that binds to a first target moiety of an analyte of interest (para. 0023, 0024, 0034, 0035), and a capture agent (sensing moiety) that binds to first detection ligand (para. 0025). Thus the sensing and signaling moieties would be in different molecules or complexes.

35. With respect to claims 54-56, Daniels et al. teach a sensor comprising a first detection reagent comprising a ligand conjugated to a semiconductor nanocrystal (signaling moiety) that binds to a first target moiety of an analyte of interest (para. 0023, 0024, 0034, 0035) which would produce fluorescence.

36. Claims 1, 2, 5-6, 8-9, 11, 12, 15-16, 19, 21, 22, 25, 26, 35-39, 48, 49, 52, 54-56 are rejected under 35 U.S.C. 102(b) as being anticipated by Blau et al. [US 2002/0048778]. Blau et al. teach an invention for detection of interaction in living cells (abstract) comprising fluorescein and rhodamine labeled EGF (sensing and signaling moieties) is added to cells for in order to detect interaction of fluorescently-labeled molecules within a cell or cell membrane using fluorescence energy transfer, which allows for the monitoring and quantitation of interactions in the cell (see entire patent).

37. In particular, with respect to claim 1, Blau et al. teach an invention for detection of interaction in living cells (abstract) comprising fluorescein and rhodamine labeled EGF (sensing and signaling moieties) is added to cells for in order to detect interaction of fluorescently-labeled molecules within a cell or cell membrane using fluorescence energy transfer (para. 0186). The fluorescein and rhodamine labeled EGF would not be naturally occurring entities.

38. With respect to claim 2, Blau et al. teach an invention for detection of interaction in living cells (abstract) comprising fluorescein and rhodamine labeled EGF (sensing and signaling moieties) is added to cells for in order to detect interaction of fluorescently-labeled molecules within a cell or cell membrane using fluorescence energy transfer (para. 0186). Thus the fluorescein and rhodamine bind indirectly to targets via the EGF receptor (para. 0046).

39. With respect to claim 5, Blau et al. teach an invention for detection of interaction in living cells (abstract) comprising fluorescein and rhodamine labeled EGF (sensing and signaling moieties) is added to cells for in order to detect interaction of fluorescently-labeled molecules within a cell or cell membrane using fluorescence energy transfer (para. 0186). The fluorescein and rhodamine labeled EGF would not be naturally occurring entities.

40. With respect to claim 6, Blau et al. teach that the invention allows for the monitoring and quantitation of interactions (para. 0070).

41. With respect to claims 8-9, Blau et al. teach that the invention utilizes fusion proteins that functions as a tracer for the binding/association reaction (para. 0088), which would therefore be de novo and products of in vitro selection. Furthermore, it is noted that the claims appear to be directed toward product-by-process limiations. "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).

42. With respect to claim 11, Blau et al. teach an invention for detection of interaction in living cells (abstract) comprising fluorescein and rhodamine labeled EGF (sensing and signaling moieties) is added to cells for in order to detect interaction of fluorescently-labeled molecules within a cell or cell membrane using fluorescence energy transfer (para. 0186). The fluorescein and rhodamine labeled EGF would not be naturally occurring entities. Blau et al. further teach that the invention allows for the monitoring and quantitation of interactions (para. 0070).

43. With respect to claim 12, Blau et al. teach an invention for detection of interaction in living cells (abstract) comprising fluorescein and rhodamine labeled EGF (sensing and signaling moieties) is added to cells for in order to detect interaction of fluorescently-labeled molecules within a cell or cell membrane using fluorescence energy transfer (para. 0186). Thus the fluorescein and rhodamine bind indirectly to targets via the EGF receptor (para. 0046).

44. With respect to claims 15-16, Blau et al. teach an invention for detection of interaction in living cells (abstract) comprising fluorescein and rhodamine labeled EGF (sensing and signaling moieties) is added to cells for in order to detect interaction of fluorescently-labeled molecules within a cell or cell membrane using fluorescence energy transfer (para. 0186). The fluorescein and rhodamine labeled EGF would not be naturally occurring entities. The fluorescein and rhodamine labeled EGF would not be naturally occurring entities. Blau et al. further teach that the invention allows for the monitoring and quantitation of interactions (para. 0070).

45. With respect to claim 19, Blau et al. teach that the invention utilizes fusion proteins that functions as a tracer for the binding/association reaction (para. 0088), which would therefore be de novo and products of in vitro selection. Furthermore, it is noted that the claims appear to be directed toward product-by-process limiations. "[E]ven though product-by-process claims are

limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).

46. With respect to claim 21, Blau et al. teach an invention for detection of interaction in living cells (abstract) comprising fluorescein and rhodamine labeled EGF (sensing and signaling moieties) is added to cells for in order to detect interaction of fluorescently-labeled molecules within a cell or cell membrane using fluorescence energy transfer (para. 0186). The fluorescein and rhodamine labeled EGF would not be naturally occurring entities. Blau et al. further teach that the invention allows for the monitoring and quantitation of interactions (para. 0070). Blau et al. teach that the invention utilizes fusion proteins that functions as a tracer for the binding/association reaction (para. 0088), which would therefore be de novo and products of in vitro selection.

Furthermore, it is noted that the claims appear to be directed toward product-by-process limiations. "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).

47. With respect to claim 22, Blau et al. teach an invention for detection of interaction in living cells (abstract) comprising fluorescein and rhodamine labeled EGF (sensing and signaling moieties) is added to cells for in order to detect interaction of fluorescently-labeled molecules within a cell or cell membrane using fluorescence energy transfer (para. 0186). Thus the fluorescein and rhodamine bind indirectly to targets via the EGF receptor (para. 0046).

48. With respect to claims 25, 26, Blau et al. teach an invention for detection of interaction in living cells (abstract) comprising fluorescein and rhodamine labeled EGF (sensing and signaling moieties) is added to cells for in order to detect interaction of fluorescently-labeled molecules within a cell or cell membrane using fluorescence energy transfer (para. 0186). The fluorescein and rhodamine labeled EGF would not be naturally occurring entities. The fluorescein and rhodamine labeled EGF would not be naturally occurring entities. Blau et al. further teach that the invention allows for the monitoring and quantitation of interactions (para. 0070).

49. With respect to claims 35-39, Blau et al. teach an invention for detection of interaction in living cells (abstract) comprising fluorescein and rhodamine labeled EGF (sensing and signaling moieties) is added to cells for in order to detect interaction of fluorescently-labeled molecules within a cell or cell membrane using fluorescence energy transfer (para. 0186), and may be used in cells such as E. coli (para. 0068), which is a chemosensory cell and would comprise methyl-accepting chemosensory receptors.

50. With respect to claim 48, Blau et al. teach an invention for detection of interaction in living cells (abstract) comprising fluorescein and rhodamine labeled EGF (sensing and signaling moieties) is added to cells for in order to detect interaction of fluorescently-labeled molecules within a cell or cell membrane using fluorescence energy transfer (para. 0186). The fluorescein

and rhodamine labeled EGF would not be naturally occurring entities. Blau et al. further teach that the invention allows for the monitoring and quantitation of interactions (para. 0070). , Blau et al. teach that the invention utilizes fusion proteins that functions as a tracer for the binding/association reaction (para. 0088).

51. With respect to claim 49, Blau et al. teach an invention for detection of interaction in living cells (abstract) comprising fluorescein and rhodamine labeled EGF (sensing and signaling moieties) is added to cells for in order to detect interaction of fluorescently-labeled molecules within a cell or cell membrane using fluorescence energy transfer (para. 0186). The fluorescein and rhodamine labeled EGF would not be naturally occurring entities. The fluorescein and rhodamine labeled EGF would not be naturally occurring entities. Blau et al. further teach that the invention allows for the monitoring and quantitation of interactions (para. 0070).

52. With respect to claim 52, Blau et al. teach that the invention utilizes fusion proteins that functions as a tracer for the binding/association reaction (para. 0088), which would therefore be products of in vitro selection.

Furthermore, it is noted that the claims appear to be directed toward product-by-process limiations. "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).

53. With respect to claims 54-56, Blau et al. teach an invention for detection of interaction in living cells (abstract) comprising fluorescein and rhodamine labeled EGF (sensing and signaling moieties) is added to cells for in order to detect interaction of fluorescently-labeled molecules within a cell or cell membrane using fluorescence energy transfer (para. 0186),

Claim Rejections - 35 USC § 103

54. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

55. Claims 4, 14, 24, are rejected under 35 U.S.C. 103(a) as being unpatentable over Daniels et al. [US 2002/0004246] in view of Lesley [US 2002/0090740].

With respect to claims 4, 14, 24, Daniels et al. teach labels such as semiconductor nanocrystals (para. 0023), as discussed above, but fail to teach labels such as enzymes wherein production of the detectable signal engenders changes in the sensor element whereby production of the detectable signal is terminated, and a change in binding of a target analyte is required to again engender production of a detectable signals.

Lesley, however, shows that enzyme and semiconductor nanocrystal labels are equivalent structures known in the art. Therefore, because these two types of labels were art-recognized equivalents at the time the invention was made, one of ordinary skill in the art would have found it obvious to substitute enzyme labels for semiconductor nanocrystals.

56. Claims 32-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Daniels et al. [US 2002/0004246] in view of Sprecher et al. [US 2003/0096339].

With respect to claims 32-34, Daniels et al. teach the invention as discussed above, including use of receptors (para. 0089). Daniels et al. do not specifically teach a four helix bundle receptor protein binding domain.

Sprecher et al., however, teach cytokine receptors that bind to four-helix bundle cytokines that play an important role in cell differentiation, activation, recruitment, and homeostasis of cells (para. 0184). Sprecher et al. further teach that cytokines are importnat in the stimulating the development of red blood cells and in restoring normal blood cell levels in patients suffering from anemia, thrombocytopenia, and neutropenia, or receiving chemotherapy for cancer (para. 0020).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to have had cytokine receptors that bind to four-helix bundle cytokines, as suggested by Sprecher et al., in the method of Daniels et al., in order to monitor the levels of cytokines in a patient, in order to determine if the patient had normal blood cell levels, and to determine whether the patient suffered from diseases such as anemia, thrombocytopenia, and neutropenia.

57. Claims 40-43, 45, 46, 48, 49, 50, 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Daniels et al. [US 2002/0004246] in view of Wun et al. [US 5,733,736].

With respect to claims 40, 41, Daniels et al. teach the invention as discussed above, including use of receptors (para. 0089). Daniels et al. do not specifically teach that the capture

agent or signaling moiety comprise a polypeptide sequence from the ligand binding domain of a bacterial methyaccepting chemosensory receptor.

Wun et al., however teach methyl-accepting chemotactic proteins such as T_{ar}, for detecting pathogens (column 5, lines 45-55) such as E.coli (column 6, lines 50-65).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to have had methyl-accepting chemotactic proteins such as T_{ar}, as suggested by Wun et al., in the method of Daniels et al., in order to monitor the presence of pathogens in a patient.

58. With respect to claim 42-43, Daniels et al. teach recombinant production of antibody fragments (para. 0148), which is a form of de novo production. The chemotactic receptors could therefore also be made using recombinant methods which are performed in vitro. Furthermore, it is noted that the claims appear to be directed toward product-by-process limiations. "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)

59. With respect to claim 45, Daniels et al. disclose a capture agent (sensing moiety) that binds to a first detection ligand (para. 0025), which would therefore bind to the target moiety indirectly.

60. With respect to claim 46, Daniels et al. teach a sensor comprising a first detection reagent comprising a ligand conjugated to a semiconductor nanocrystal (signaling moiety) that binds to a first target moiety of an analyte of interest (para. 0023, 0024, 0034, 0035), and a capture agent

(sensing moiety) that binds to first detection ligand (para. 0025). Daniels et al. also teach a second detection reagent that is capable of selectively binding a second target moiety of the analyte of interest (para. 0035). Therefore different labels could bind to the different capture agents.

61. With respect to claims 48, 49, Daniels et al. teach a sensor comprising a first detection reagent comprising a ligand conjugated to a semiconductor nanocrystal (signaling moiety) that binds to a first target moiety of an analyte of interest (para. 0023, 0024, 0034, 0035), and a capture agent (sensing moiety) that binds to first detection ligand (para. 0025). Daniels et al. also teach a second detection reagent that is capable of selectively binding a second target moiety of the analyte of interest (para. 0035). It is noted that the semiconductor nanocrystals are not a naturally occurring entity. Therefore, the sensor taught by Daniels et al. would be capable of detecting a first and second target analyte using different labels. Daniels et al. further teach detecting multiple analytes of interest and further quantitating the amount of a particular analyte present (para. 0121).

62. With respect to claim 50, Daniels et al. teach detecting multiple analytes of interest and further quantitating the amount of a particular analyte present (para. 0121). Therefore, the sensor of Daniels et al. would be capable of detecting first and second analytes of different concentrations.

63. With respect to claim 57, Daniels et al. teach a sensor comprising a first detection reagent comprising a ligand conjugated to a semiconductor nanocrystal (signaling moiety) that binds to a first target moiety of an analyte of interest (para. 0023, 0024, 0034, 0035) which would produce fluorescence.

64. Claim 44 is rejected under 35 U.S.C. 103(a) as being unpatentable over Daniels et al. [US 2002/0004246] in view of Wun et al. [US 5,733,736], as applied to claim 43 above, and further in view of Wang et al. [US 2001/0051855].

With respect to claim 44, Daniels et al. and Wun et al. teach the invention as discussed above, but fail to teach directed evolution to produce the de novo designed patterned sequence polypeptide sequence.

Wang et al., however teach that in vitro directed evolution of biopolymers such as proteins allows for improvements to be obtained while minimally disrupting a desired biopolymer property such as stability or functionality.

Therefore, it would have been obvious to one of ordinary skill in the art to have used directed evolution techniques, as suggested by Wang et al. to produce the polypeptide sequences of Daniels et al. and Wun et al., in order to obtain the desired polypeptide while minimally disrupting desired biopolymer properties such as stability or functionality.

65. Claim 47 is rejected under 35 U.S.C. 103(a) as being unpatentable over Daniels et al. [US 2002/0004246] in view of Wun et al. [US 5,733,736], as applied to claim 40 above, and further in view of Lesley [US 2002/0090740].

With respect to claim 47, Daniels et al. teach labels such as semiconductor nanocrystals (para. 0023), as discussed above, but fail to teach labels such as enzymes wherein production of the detectable signal engenders changes in the sensor element whereby production of the

detectable signal is terminated, and a change in binding of a target analyte is required to again engender production of a detectable signals.

Lesley, however, shows that enzyme and semiconductor nanocrystal labels are equivalent structures known in the art. Therefore, because these two types of labels were art-recognized equivalents at the time the invention was made, one of ordinary skill in the art would have found it obvious to substitute enzyme labels for semiconductor nanocrystals.

66. Claims 58 is rejected under 35 U.S.C. 103(a) as being unpatentable over Daniels et al. [US 2002/0004246] in view of Wun et al. [US 5,733,736] as applied to claim 40 above, and further in view of Kelso [US 2003/0129296].

With respect to claim 58, Daniels et al. and Wun et al. teach fluorescent labels such as semiconductor nanocrystals, as discussed above, but fail to teach FRET labels.

Kelso, however, teaches that labels may comprise quantum dots (which are semiconductor nanocrystals) (para. 0072) as well as energy transfer conjugates (para. 0078), which may be used in FRET assays. Kelso thus shows that semiconductor nanocrystals and energy transfer conjugates are equivalent structures known in the art.

Therefore, because these two were art-recognized equivalents at the time the invention was made, one of ordinary skill in the art would have found it obvious to substitute FRET conjugate labels for semiconductor nanocrystals in the sensor of Daniels et al.

Conclusion

67. No claims are allowed.

68. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nelson Yang whose telephone number is (571)272-0826. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571)272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

69. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Nelson Yang/
Patent Examiner, Art Unit 1641